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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/722,703	11/25/2003	Jian Jeffrey Chen	R0085D-CON	7431

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EXAMINER	
BALLS, ROBERT J	

ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 03/14/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/722,703	CHEN ET AL.	
	Examiner	Art Unit	
	James Balls	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *60-77* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *60-75* is/are allowed.

6)☒ Claim(s) *76 and 77* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

1. Claims 60 – 77 are pending.

2. This application is a divisional application of U.S. Patent Application Ser. No. 10/073,845 filed on February 11, 2002 (now U.S. Patent No. 6,696,566), and claims the benefit of U.S. Provisional Application Nos. 60/268,375 filed on February 12, 2001 and 60/334,654 filed on November 30, 2001.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. §112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 76 is rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Claim 76 does not enable one of ordinary skill in the art to practice the invention without undue experimentation. The following factors set out in *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1998), are used to determine whether undue experimentation is required: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The

amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure.

(A) The claim is broad due to the high number of compounds and diseases it embodies. Formula I encompasses many different compounds based on the high number and breadth of its variables (i.e. R^1, R^2, R^3, X^1 and Ar^1). Although the scope of the diseases covered by the claim is unclear (see the rejection under 35 U.S.C. §112, second paragraph), for purposes of this analysis, the list of diseases on pages 29-31 is assumed. A wide variety of diseases are listed, including: inflammation, retinopathies, cancer, gastrointestinal conditions, cardiovascular diseases, autoimmune disorders, liver disease, disorders of the female reproductive system, irritable bowel syndrome, lupus, septic shock, bone resorption diseases, nephritis, burns, diabetes, Alzheimer's disease, scar tissue formation, and cachexia (just to name a few). The list of seemingly unrelated disorders spans three pages of the specification.

(B) The invention is directed toward pharmaceuticals and treating diseases employing said pharmaceuticals, an art which is highly unpredictable. "[T]he scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(C) The specification provides limited direction or guidance in terms of using the claimed compounds to treat all the diseases listed in the specification.

Only generic dosage information is provided, which is not linked to any specific diseases.

(D) The state of the prior art demonstrates that the probability of claimed compounds working to treat each disease listed in the specification is extremely low. Boehm & Adams in *New Inhibitors of p38 Kinase*, explain that there is very little knowledge relating to these compounds and whether they actually work to treat diseases. Boehm & Adams, *New Inhibitors of p38 Kinase*, Exp. Opin. Ther. Patents 10(1):25-37 (2000). In the last paragraph of page 34, Boehm & Adams explain that cellular data exists that suggests potential involvement of p38 in disease such as "stroke, myocardial ischemia, Alzheimer's disease, osteoarthritis and lung injury." However, suspecting involvement with a particular disease is not tantamount to actually demonstrating how to use a claimed compound to treat that disease.

(E) The specification is void of working examples demonstrating how to treat a disease with the claimed compounds.

(F) The skill of those in the art varies widely based on the nature of the disease. The disorders in the specification include malaria where the skill level is very high and disorders where the skill level is low, such as irritable bowel syndrome (treatment is nutritional, i.e. adding fiber to the diet).

(G) The quantity of experimentation necessary to make or use the disclosed invention is very high based on the breadth of the claims, the unpredictability of the art, limited guidance in the specification, lack of working examples, and the skill of those in art.

4. Claim 77 is rejected under 35 U.S.C. §112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter that was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. The specification does not enable one of ordinary skill in the art to practice the invention as claimed. Again, the *In re Wands*-analysis is employed.

(A) Claim 76 is broad due to the high number of compounds and diseases it embodies. Formula I encompasses many different compounds based on the high number and breadth of its variables (i.e. R^1, R^2, R^3, X^1 and Ar^1). Claim 77 contains a number of seemingly unrelated diseases, arthritis, Crohns disease, irritable bowel syndrome, adult respiratory distress syndrome or chronic obstructive pulmonary disease.

(B) The invention is directed toward pharmaceuticals and treating diseases employing said pharmaceuticals, an art which is highly unpredictable. "[T]he scope of enablement varies inversely with the degree of unpredictability of the factors involved," and physiological activity is generally considered to be an unpredictable factor. *In re Fisher*, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970).

(C) The specification provides limited direction or guidance in terms of using the claimed compounds to treat all the diseases listed in Claim 77. Only generic dosage information is provided, which is not linked to any specific diseases.

(D) The state of the prior art demonstrates that the probability of claimed compounds working to treat each disease listed is extremely low. Boehm & Adams in *New Inhibitors of p38 Kinase*, explain that there is very little knowledge relating to these compounds and whether they actually work to treat diseases. Boehm & Adams, *New Inhibitors of p38 Kinase*, Exp. Opin. Ther. Patents 10(1):25-37 (2000). In the last paragraph of page 34, Boehm & Adams explain that cellular data exists that suggests potential involvement of p38 in diseases such as "stroke, myocardial ischemia, Alzheimer's disease, osteoarthritis and lung injury." However, suspecting involvement with a particular disease is not tantamount to actually demonstrating how to use a claimed compound to treat that disease.

(E) The specification is void of working examples demonstrating how to treat a disease with the claimed compounds.

(F) The skill of those in the art varies widely based on the nature of the disease. The disorders in Claim 77 include arthritis where the skill level is very high and disorders where the skill level is low, such as irritable bowel syndrome (treatment is nutritional, i.e. adding fiber to the diet).

(G) The quantity of experimentation necessary to make or use the disclosed invention is very high based on the breadth of the claims, the unpredictability of the art, limited guidance in the specification, lack of working examples, and the skill of those in art.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. §112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claim 76 is rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 76 is drawn to a method of treating a p38-mediated disorder. However, a "p38 mediated disorder" is not commonly recognized category of disease, and therefore the metes and bounds of claim 76 are unclear. The specification defines a p30 mediated disorder on page 31, line 13 as:

> "[a disorder referring] to any and all disorders and disease states in which p38 plays a role, either by control of p38 itself, or by p38 causing another factor to be released, such as but not limited to IL-1, IL-6 or IL-8. A disease state in which, for instance, IL-1 is a major component, and whose production or action, is exacerbated or secreted in response to p38, would therefore be considered a disorder mediated by p38."

It is unclear which diseases fall within this definition of p38-mediated diseases. For example, suppose that one patient with a disease responds to a compound of Formula I but another patient with the same disease does not respond to that compound. It is unclear whether Claim 76 would encompass that disease. Also, suppose that a compound of Formula I is effective at treating a disease only when combined with another compound. Again, it is unclear whether Claim 76 would include that disease. Thus, the claim does not particularly point out and distinctly claim the subject matter that the applicant regards as his invention.

Conclusion

6. Claims 60 – 75 are allowable.

7. Claims 76 and 77 are rejected under 35 U.S.C. §112.

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to James Balls whose telephone number is (571) 272-7997. The examiner can normally be reached on Mon - Fri 8:00am - 4:30pm EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cecilia Tsang can be reached on (571) 272-0562. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

James Balls
Examiner
Art Unit 1625

Cecelia Tsang
Supervisory Patent
Art Unit 1625